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EXAMINER	
BOWERS, NATHAN ANDREW	

ART UNIT	PAPER NUMBER
1797	

NOTIFICATION DATE	DELIVERY MODE
06/15/2010	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)	
	10/525,549	WIKSWO ET AL.	
	Examiner	Art Unit	
	NATHAN A. BOWERS	1797	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *05 April 2010*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-16,19-48 and 50-65* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-16,19-48 and 50-65* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

1) Claims 1-5, 8-16, 19-22, 33-38, 41-48 and 50-65 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kanegasaki (US 20030003571) in view of Hanagan (US 5520787) and Breznak (US 5589352).

With respect to claim 1, 15, 16, 19-22, 33, 45-48, 50-52 and 57-65, Kanegasaki discloses a cell motion analysis system comprising a first substrate (Figure 5:7) having first and second surfaces defining a chamber therebetween. A barrier comprising a channel (Figure 5:1) and a plurality of protrusions (Figure 5:6) serve to divide the chamber into a first subchamber (Figure 5:2A) and a second subchamber (Figure 5:2B). This is disclosed in paragraphs [0084], [0085] and [0095]. Paragraph [0097] states that the protrusions and grooves formed within the channels are varied in order to control the diffusion of a particular cell type between the subchambers. Paragraph [0121] states that the gaps of the barrier range from 3 to 50 microns. Figure 12 and paragraph [0112] describe another configuration in which first and second barriers (1) are positioned so as to form a central chamber (2A), an intermediate chamber (2B), and an outer chamber (2C). Furthermore, Kanegasaki indicates that a second substrate (Figure 6:9) is positioned adjacent to a first surface of the first substrate (Figure 6:7), and that a third substrate (Figure 6:8) is provided in communication with a second surface of the first substrate (Figure 6:7). Kanegasaki, however, does not expressly disclose that the apparatus is capable of cultivating living cells, or that the third substrate includes a means for electrochemical measurements.

Breznak discloses a system similar to that of Kanegasaki in that it is used to measure the chemotactic response of a cell to a chemical. This is described in column

4, line 63 to column 5, line 22 and column 9, line 20 to column 10, line 4. Column 5, lines 22-50 further state that the chemotaxis chamber of Breznak is further adapted to facilitate and monitor cell growth.

Hanagan discloses an apparatus for monitoring cell growth and activity by measuring the concentration of various analytes in the culture solution. Hanagan discloses that a plurality of electrodes (Figure 1:30) are positioned apart from each other so that each electrode is in communication with a flow channel (Figure 1:66) capable of carrying a liquid to be tested. Column 2, lines 8-10 and column 6, lines 35-40 state that the presence of multiple analytes (i.e. glucose and oxygen) are simultaneously detected using different enzymes immobilized on multiple electrodes. The use of counter electrodes, reference electrodes, edge connector pads (Figure 3:350) and electrically conductive leads (Figure 3:360) is disclosed in the abstract and column 8, lines 43-54.

.Kanegasaki, Breznak and Hanagan are analogous art because they are from the same field of endeavor regarding cell detection systems.

At the time of the invention, it would have been obvious to ensure that the Kanegasaki chemotaxis apparatus is adapted to additionally facilitate and monitor cell growth. Breznak is evidence that it is well known in the art to encourage and monitor cell growth while simultaneously detecting the cellular response to a chemotactic compound. Hanagan further teaches that cell growth may be detecting by providing a plurality of electrodes capable of electrochemically detecting metabolic analytes in solution. Incorporation of this electrochemical measuring system of Hanagan into the

apparatus of Kanegasaki would allow for a second means to determine cell behavior in addition to simple visual observation. Hanagan teaches that electrical detection using a patterned array of electrodes offers a rapid, automated and multiplexed analysis of cell culture analytes in real time.

With respect to claims 2 and 34, Kanegasaki, Hanagan and Breznak disclose the bioreactor set forth in claims 1 and 33. As noted above, Kanegasaki teaches that barriers are located between the first and second subchambers, and are adapted for allowing the perfusion of certain cell types while restricting the movement of certain cell types.

With respect to claims 3-5 and 35-38, Kanegasaki, Hanagan and Breznak disclose the bioreactor set forth in claims 2 and 33. The Kanegasaki bioreactor is considered to be fully capable of accommodating any type of microorganism including bacteria, protozoa, tumor cells, endothelial cells, and normal tissue cells.

With respect to claims 8 and 9, Kanegasaki, Hanagan and Breznak disclose the bioreactor set forth in claim 1. Additionally, Kanegasaki teaches that an input port (Figure 3:3Aa) and an input transfer channel are formed in the substrate and provided in fluid communication with the first subchamber. Furthermore, an outlet port (Figure 3:3Ba) and an outlet transfer channel are provided in communication with the second subchamber.

With respect to claims 10 and 11, Kanegasaki, Hanagan and Breznak disclose the bioreactor set forth in claim 9 wherein at least one auxiliary port and channel are provided in fluid communication with the input and outlet ports. Kanegasaki teaches that additional ports (Figure 3:4Ba and Figure 3:4Aa) are used in conjunction with inlet (Figure 3:3Aa) and outlet (Figure 3:3Ba) ports, so as to supply extra reagents to the subchambers.

With respect to claims 12 and 13, Kanegasaki, Hanagan and Breznak disclose the bioreactor set forth in claim 11. As previously noted above, Kanegasaki indicates that a second substrate (Figure 6:9) is positioned adjacent to a first surface of the first substrate (Figure 6:7). The second substrate comprises a plurality of connection channels (Figure 6:3A, 4A, 4B, 3B) that are aligned with the inlet/outlet ports of the first substrate.

With respect to claims 14 and 44, Kanegasaki, Hanagan and Breznak disclose the bioreactor set forth in claims 1 ad 33 wherein the first substrate is formed from silicon. This is described in paragraph [0154] of Kanegasaki.

With respect to claims 23 and 24, Kanegasaki, Hanagan and Breznak disclose the apparatus set forth in claim 17. Kanegasaki additionally describes the use of silicon substrates in paragraph [0154].

With respect to claims 41-43, Kanegasaki, Hanagan and Breznak disclose the bioreactor set forth in claim 33. Kanegasaki further indicates that inlet and outlet ports (Figure 12:3a, 4a) are provided for each of the external, central, and intermediate chambers.

With respect to claims 53-56, Kanegasaki, Hanagan and Breznak disclose the apparatus set forth in claim 52. The plurality of electrodes disclosed by Hanagan are fully capable of being subdivided into any number of subgroups. The creation of second and third electrode groups would not require any change in the structure of the device, but would merely require a change in the experiment protocol. Altering the controller program does not result in a structurally significant limitation in an apparatus claim, but rather represents an intended use.

2) Claims 25-32 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kanegasaki (US 20030003571), Hanagan (US 5520787) and Breznak (US 5589352) as applied to claim 1, and further in view of Allen (US 20040142409).

Kanegasaki, Hanagan and Breznak disclose the apparatus set forth in claim 1 as set forth in the 35 U.S.C. 103 rejection above. Although Kanegasaki discloses in paragraphs [0163]-[0165] an optical system for the interrogation of motile cells, Kanegasaki does not indicate that the optical sensors and light sources are provided on a substrate above the first substrate.

Allen discloses a detection system for monitoring the movement and presence of a cell (Figure 1:56) in a solution. An upper substrate (Figure 1:25) is provided above the base substrate (Figure 1:10), and serves to house a light source (Figure 1:30) and a photodetector (Figure 1:40). This is described in paragraphs [0033]-[0035].

Kanegasaki and Allen are analogous art because they are from the same field of endeavor regarding optical means for monitoring cell movement in a microfluidic system.

At the time of the invention, it would have been obvious to provide the Kanegasaki device with an additional substrate capable of holding a plurality of optical sensors, LED light sources and other optical detection means well known in the art. By arranging all critical optical components on an independent substrate, the overall apparatus would be characterized by a modular construction that would allow one to add and remove the optical devices with greater ease. As evidenced by Allen, it is well known in the art to form important detection means integral with a substrate formed above a culture chamber.

3) Claims 6, 7, 39 and 40 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kanegasaki (US 20030003571), Hanagan (US 5520787) and Breznak (US 5589352) as applied to claims 1 and 33, and further in view of Thomas (US 20060194273).

Kanegasaki, Hanagan and Breznak disclose the apparatus set forth in claim 33 as set forth in the 35 U.S.C. 103 rejection above, however do not expressly disclose the use of cell adhesion coatings.

Thomas discloses the bioreactor as previously described above. In paragraphs [0040] and [0042], Thomas teaches that biocompatible coatings are applied to the surfaces of the cell chamber in order to promote cell adhesion.

Kanegasaki and Thomas are analogous art because they are from the same field of endeavor regarding microfluidic bioreactors.

At the time of the invention, it would have been obvious to utilize the adhesion promoting coatings disclosed by Thomas in the apparatus set forth by Kanegasaki. In paragraph [0160], Kanegasaki teaches that materials that encourage cell adhesion to substrate surfaces are beneficial. One of ordinary skill in the art would have recognized that the application of a coating to the substrate of Kanegasaki would have required only minor structural alterations, and would be completed in a predictable manner while yielding predictable results.

Response to Arguments

Applicant's arguments filed 05 April 2010 with respect to the 35 U.S.C. 103 rejections involving Kanegasaki and Hanagan have been fully considered and are persuasive. Therefore, these rejections have been withdrawn. However, upon further consideration, a new ground of rejection is made in view of the combination of Kanegasaki, Hanagan and Breznak.

The Breznak reference is provided as evidence that one of ordinary skill would have been motivated to measure cell growth when monitoring the chemotactic response of a cell population. Breznak teaches that it is important to measure cell growth and cell movement at the same time within a common chamber. Accordingly, one of ordinary skill would have found it obvious to ensure that the Kanegasaki chamber is not only capable of measuring chemotaxis, but also is capable of facilitating microorganism culture through the introduction of necessary nutrients and gases. It would have been apparent to measure cell growth using conventional detection devices, such as the electrochemical measuring system of Hanagan.

Conclusion

This is a non-final rejection.

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to NATHAN A. BOWERS whose telephone number is (571)272-8613. The examiner can normally be reached on Monday-Friday 7 AM to 4 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Marcheschi can be reached on (571) 272-1374. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Nathan A Bowers/
Examiner, Art Unit 1797